ABSTRACT. There is a notion that tolerance is an inevitable complication when patients are maintained on opioid analgesic regimens for an extended period of time. Whether this is true or not, it is important to remember that, in spite of growing regulatory scrutiny and spreading fear around these medications, defining “ceiling doses” of opioids has more to do with clinician comfort and much less to do with reality and patient requirements. This commentary posits that clinicians must return to the principles of balancing efficacy with toxicity as the dose-limiting factor once again, contextualized by outcomes in the areas of function and compliant drug-taking.

KEYWORDS. Opioid, tolerance, dose, addiction

The preceding commentary entitled “Opioid Tolerance from the Perspective of Person with Pain” is important because it touches upon many of the key issues that influence—mainly for the worse—the management of the need for increasing opioid doses in patients with chronic pain. Tolerance is poorly understood, difficult to recognize, and often requires a well thought-out, multidimensional response from clinicians who have limited time to develop one. We argue that it isn’t entirely important—the number of milligrams is irrelevant (at least it used to be!) and the way in which the request for an increase in dose is handled is individualized and goes on within a context of a multidimensional assessment regardless of whether it is driven by tolerance or other factors. The clinician assessing such situations must recognize that the underlying pathology of the pain may be worsening when an opioid medication is no longer working well—especially in cancer patients.

During a recent discussion about opioid therapy with a pain management physician friend and colleague, we talked about the fact that physicians in the 1990s supported the use of high dose therapy more than is currently the case. He referred to that time period as the “no ceiling” days. He was referring to the thinking that surrounded opioid use for managing nonmalignant pain in which the principle of titration of dose to efficacy or toxicity ruled the day. When applied in a certain fashion, this led to more pa-
tients receiving higher opioid doses than is the norm today. The use of high dose opioid therapy was mainly supported by clinical experience in cancer pain management and end-of-life care. Whether driven by increasing pathology, tolerance, or other factors, clinicians had an explanatory model and a sense of security about medical-legal issues, gave the benefit of the doubt to the patient, and increased doses more readily. For non-cancer pain, the use of high doses was largely supported by anecdotal clinical experience; this admittedly reflects not much evidence, although the abandonment of the practice today is based on little more. Thus, important questions arise:

- Was every patient helped by this practice of using high opioid doses? Certainly not.
- Were some? Certainly yes.
- Did some people get the doses they needed to keep on functioning? Yes.
- Did some get enough rope to hang themselves with? Yes—with regard to running into problems of toxicity and even abuse.

The fact is, no single practice or model benefits all of the tremendously diverse population of people in chronic pain and the writer correctly points out that ambivalence about this practice is based in large part on non-medical factors.

With the souring of the regulatory climate and the growth of prescription drug abuse, there has been a trend for clinicians to shy away from using high opioid doses. Many now respond to the need to repeatedly increase opioid doses with rotation to another opioid. This practice is based upon incomplete cross tolerance or genetic polymorphic effects that appear to make some patients more sensitive to certain opioids than to others. Hopefully this practice helps to balance efficacy and toxicity. Some clinicians set arbitrary dose limits for various opioids. Others have stopped using certain opioids that they perceive as presenting higher risk or street value—although evidence to support those contentions is usually lacking. Still others have become so disillusioned that they have stopped using opioids altogether.

My (SDP) initial response to my pain management physician friend was that those good (bad?) old days were not the “no ceiling” days but more the “no context days.” Mu agonist opioid analgesics, pharmacologically speaking, still have no a priori dose ceiling. Cancer patients and those with progressive disease can still be treated with increasing doses and doses can still be titrated to effect or toxicity with no arbitrary number of milligrams constituting a limit. The same is still true for certain, carefully selected, non-cancer pain patients. The key words are “carefully selected” and the decision to apply the principle of titration to efficacy or toxicity is based upon the examination of the clinical context—namely a review of the 4 A’s (analgesia, activity, adverse effects and aberrant drug taking behavior).3–6

Consider the following two case examples:

Mr. Smith, 28 years old and on disability from his factory job due to an injury, is taking 160 mg of sustained release oxycodone twice daily for his low back pain. His pain is presently 8/10 (on a 10 point pain intensity scale for which 0 represents no pain and 10 the worst pain he can imagine), but he had been in less pain on the same dose for several months. He reports that before therapy his pain was 10/10 and he was unable to get off the couch. He has been able to help his wife with some household chores, returned to church services this past weekend, and has made some calls about getting his GED high school equivalency diploma. He has some constipation but is responding to a bowel regimen. He has never run out of his opioids early and has had consistently clean urine toxicology screens. He is requesting an increase in the oxycodone.

Mr. Jones, 28 years old and on disability from his factory job due to an injury, is also taking 160 mg of sustained release oxycodone twice daily for his low back pain. His pain is presently 8/10 (on a 10 point pain intensity scale for which 0 represents no pain and 10 the worst pain he can imagine), but he had been in less pain on the same dose for several months. He reports that before therapy his pain was 10/10 and he was unable to get off the couch. He has been able to help his wife with some household chores, returned to church services this past weekend, and has made some calls about getting his GED high school equivalency diploma. He has some constipation but is responding to a bowel regimen. He has never run out of his opioids early and has had consistently clean urine toxicology screens. He is requesting an increase in the oxycodone.
pain control and reduces his nausea. He is requesting an increase in the oxycodone.

Why do Mr. Smith and Mr. Jones hurt so badly again? Is it due to tolerance, more activity, more inactivity, emotional issues, drug abuse, or diversion? This is a very difficult question to sort out. Yet where the clinician would likely increase the oxycodone versus discontinuing it, rotate opioids, add additional “structure,” and make additional referrals seems relatively obvious in today’s pain practice. It might be unlikely in today’s climate for either patient to receive an increase as requested, but Mr. Smith is certainly more apt to realize that goal. While pain levels might remain elevated (and this may be the case for many reasons, including a genuine fear that the medication might be decreased or taken away from them if they show too much improvement), Mr. Smith is exhibiting adequate analgesia, but more importantly his activities of daily living are increasing. Patients who begin to reengage with life are very unlikely to be “bad” or “addicted” patients (at least for any length of time). Further, Mr. Smith is having adverse side effects but reporting that they are adequately managed. Rounding out the 4 A’s, Mr. Smith has no obvious aberrant drug-related behaviors as evidenced by his urine drug findings and never running out of medication early.

Placing that same 4 A’s magnifying glass on Mr. Jones tells another story. While his pain reports mimic Mr. Smith, Mr. Jones is less functional and seems to be holding the physician ransom in this regard (i.e., “I’ll only be able to get moving when I get more medicine from you . . .”). His adverse side effects are somewhat managed, but he is explaining his marijuana use partially by stating it is for his nausea. What will an oxycodone dose increase, as requested, do for the patient in this regard? Finally, Mr. Jones is clearly displaying aberrant drug-taking behaviors which need to be addressed. While running out of his opioids early and his use of marijuana does not necessarily indicate addiction, these are sure signs that more structure and careful monitoring is indicated for Mr. Jones. At this particular stage in time, he would not be a good candidate for an increase in his oxycodone.

The 4 A’s contextualize the principle of titration to efficacy versus toxicity and thus the interpretation of the need for a dose increase. If a patient presents an acceptable picture in each domain of the 4 A’s, as described by the case of Mr. Smith, we can proceed with dose escalations (along with careful documentation). However, if the patient is “toxic” in any of the domains, more caution needs to be exercised and alternate methods need to be explored before proceeding. Even this, however, should not preclude the eventual increase in dose if the various domains can be brought back into line. As pragmatic psychologists, the numbers of milligrams or micrograms mean nothing to us. Restoring lives, helping people function, giving them a sense of meaning and peace, and avoiding harming people with pain are our main considerations. We are treating people, not massaging numbers.

REFERENCES


doi:10.1300/J354v21n01_09